## REMARKS

Claims 1-18 are currently pending in the application. Claims 1 and 7 are amended. Claims 15-18 are added. The amendment and new claims find support in the specification and are discussed in the relevant sections below. No new matter is added.

Priority Claim

Applicants thank the Examiner for his acknowledgment of Applicants' claim for priority, including the foreign priority based on PCT/GB99/01956, filed on 6/23/1999 and GB9813531.2, filed on 6/23/1998. Applicants enclose a certified copy of each of the above priority applications pursuant to 35 U.S.C. 119(b). Applicants believe that the priority claim to these two applications is perfected with the submission of the certified copies, and respectfully request confirmation of such perfection.

The present application also claims priority to U.S. Provisional Application 60/090,867, filed June 26, 1998, as acknowledged in the filing receipt dated October 9, 2001.

Rejections under 35 U.S.C. 112, Second Paragraph

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because of insufficient antecedent basis for the recitation of "the unmasking of the second region."

Applicants have amended claim 7 to recite "said second region is unmasked in the presence of said target nucleic acid molecule." The amendment is supported by the original claim 7 and in the specification, e.g., on page 7, lines 18-19.

Applicants believe the amendment to claim 7 obviates the rejection under 35 U.S.C. 112, second paragraph, and respectfully requests that it be withdrawn.

Rejections under 35 U.S.C. 102(b)

Claims 1-14 are rejected under 35 U.S.C. 102(b), alleged as being anticipated by Agrawal et al. (WO 94/01550). The Examiner states that Agrawal et al. discloses "antisense that have a

first region and a second region that bind a target sequence wherein the first region is available for binding while the second region is temporarily 'masked'." The Examiner specifically refers to page 7 of the Agrawal et al. reference and Figures 1, 2, 5, and 6 which allegedly disclose the "masking through a hairpin structure." According to the Examiner, Figure 1 discloses that the "self-complementary region/second region is complementary to a sequence of the target sequence that is contiguous with that targeted by a first region/hybridisations region." The Examiner concludes that Agrawal et al. anticipates claims 1-14 of the present invention.

Although Applicants do not acquiesce to the Examiner's rejection, they have amended claim 1 to require that the first region be "*of insufficient length to form a stable hybrid with the target molecule.*" The amendment finds support in the specification, for example, at page 9, lines 2 to 4.

Agrawal et al. teaches self-stabilised oligonucleotides which are more stable than conventional antisense molecules due to formation of a hairpin structure that resists nucleolytic degradation. Agrawal et al. does not, however, teach an antisense nucleic acid molecule having distinct first and second hybridisation regions, wherein the first region is "*of insufficient length to form a stable hybrid with said target nucleic acid molecule,*" as required by the amended claims. To the contrary, Agrawal et al. teaches an oligonucleotide having a first targeting region which is *capable of forming a stable hybrid with its target*, and a second self-complementary region that protects the molecule from degradation. In other words, it is this portion of the Agrawal molecule, the first targeting region, which is primarily responsible for forming the hybrid structure with the target gene. For example, Agrawal et al. states that the "targeting region" is capable of hybridising to the target region under physiological conditions such that interference with the function of the cellular sequence is observed (see page 10, lines 1-13). Thus, the Agrawal et al. references teaches an oligonucleotide having (1) a first targeting region that hybridises to the target sequence to mediate the biological effect of the antisense molecule, and (2) a second self-complementary region that protects the molecule from nucleolytic degradation. Nowhere in this reference is there any teaching or suggestion of an antisense molecule having two separate targeting regions, one of which is independently incapable of hybridising to the target sequence, and thus both of which targeting regions are required for biological activity.

Applicants therefore respectfully request the 102(b) rejections on claims 1-14 be withdrawn.

New Claims 15-18

Claims 15-18 are newly added. Support for such addition can be found in the originally filed claims and throughout the specification, e.g., on page 6, line 29; page 7, line 3; page 8, lines 16-32; and page 9, lines 6-11.

As a result of this amendment, claims 1-18 are currently pending. Applicant submits that all pending claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

Date: March 24, 2004

Name: Barbara A. Gyure
Registration No.: 34,614
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100